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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/575,136

05/09/2007

Amos B. Smith III

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EXAMINER

CHANDRAKUMAR, NIZAL S

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

06/26/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/575,136	Applicant(s) SMITH ET AL.	
	Examiner NIZAL S. CHANDRAKUMAR	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 April 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-83 is/are pending in the application.
- 4a) Of the above claim(s) 29-83 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>02/28/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This application is a 371 of PCT/US04/33473 10/12/2004
which claims benefit of 60/510,097 10/09/2003

Election/Restrictions

Applicant's election of Group III claims 1-28 in the reply filed on 04/20/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 29-83 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 04/20/2009.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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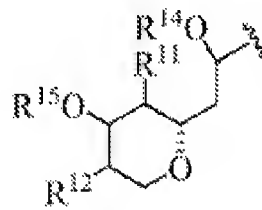
art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and dependent claims 2-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the relevant factual considerations. Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: (1) breadth of the claims; (2) nature of the invention; (3) state of the prior art; (4) amount of direction provided by the inventor; (5) the level of predictability in the art; (6) the existence of working examples; (7) quantity of experimentation needed to make or use the invention based on the content of the disclosure; and (8) relative skill in the art.

All of the factors have been considered with regard to the claims, with the most relevant factors discussed below:

The invention relates to compounds which mimic the chemical and/or biological activity of discodermolide and to methods and intermediates useful in their preparation. It is stated on page 3, line 1, that there is need for *improved* synthetic methods for making compounds of formula I. The claims are drawn to a process of making lactones and tetrahydropyran (THP) compounds of formula I, consisting of the reaction of intermediate XX (which has this lactone or THP group) with

intermediate i. (Note: claims 1-21 drawn to lactones and THPs; claims 1 and claims 22-28 are drawn to lactones) The direction, guidance and working examples in the specification is limited to the preparation of the intermediate i. As to the making of intermediate XX, the disclosure is limited, incomplete, and is in the form of a synthetic scheme on page 33-34. There is no working example corresponding to this scheme for making intermediates XX. Though a compound BC corresponding to a lactone compound XX is used in Example 11, there is no working example disclosed on how this intermediate was made. There is no citations (literature or commercial) of prior art reference that could be usable in lieu of a working example. Further, it is not seen



where disclosure with regards to making THP versions of J is found in the specification. One skilled in the art would anticipate that the scheme on page 33 for making lactonic intermediate XX is not extendable to making such THP intermediate. Such an extension (see page 33 scheme for Fragment C) would entail undue amount of research effort to arrive at viable protection/deprotection strategies of several similar hydroxyl groups, and reduction/oxidation methods for similar carbonyl functionalities, as well as stereo-controlled synthetic methods (assuming appropriate chiral starting materials are available). Further there is no enabling disclosure in the specification for converting a lactone of the formula I (for example as found in discodermolide) to the corresponding THP compound of formula I. In addition, in the scheme 6, page 35, the reaction using alumina (Al₂O₃, see the

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penultimate step) is incompletely disclosed. This reagent, stated as a 'hydrolyzing agent' in the making of compound of formula II (see claims 26-28, and specified as alumina in claim 28), is claimed as needed for making a carbamoyl group from a hydroxyl group. One skilled in the art would anticipate that the an additional, **H** contributing agent is needed to convert an OH containing compound (using Cl_3CCONCO) to a CONH_2 group; also note that it is common knowledge that alumina is used in dehydration processes and not in hydration processes. Thus for example, one skilled in the art would anticipate a hydroxyl containing solvent in this reaction would compete with trichloromethylisocyanate reagent; any conceivable aluminum containing reaction intermediate would require hydrolysis with a proton donor to provide the carbamoyl group. There is no working example in the specification for such a transformation. There is also no teaching in the form of prior art citations for such a reaction. It is acknowledged that a 112-1 scope-of-enablement rejection (as opposed to 112-1 enablement rejection) could have been presented in view of the use of lactone BC in Example 11. However, it is noted the BC relates to one of the two intermediates mandatory for the claimed process. The unpredictability in the art of organic synthesis is high in spite of the high skill level in the area. The state of the art of organic chemical synthesis is closer to what is described by Dorwald et al. who states, "Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are". Dorwald F. A. Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface pg. 1-15. For these reasons there is a

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substantial gap between what is taught in the specification and what is being claimed. As such, one of ordinary skill in the art would be faced with undue amount of experimentation to arrive at viable synthetic methods to make intermediates XX which could be used to make compounds of formula I, let alone arriving at 'improved' methods.

Claims 1-28 are not allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NIZAL S. CHANDRAKUMAR whose telephone number is (571)272-6202. The examiner can normally be reached on 8.30 AM - 4.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571 0272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nizal S Chandrakumar/
Examiner, Art Unit 1625